REMARKS

The Office Action rejected claims 1-9, 11-28 and 34-43. The application continues to include claims 1-9, 11-28 and 34-43. Applicant would first like to address the Office Action's response to applicant's arguments presented in the Response to the Advisory Action (dated March 8, 2005). In particular, the Office Action discusses (bottom of page 3 continuing on to page 4) how "the present claims do not exclude groups of the bridges being reactive with primary nitrogens of tissue", and even if the claims were so limited, the term "generally non-reactive" would "not exclude some reaction of bridge groups with tissue." Applicant's attorney does not understand how this has any bearing on the patentability of the claims. Applicant's attorney has not argued this point. It is believed that the claim language "the bridges being generally non-reactive with other bridges" distinguishes the invention of this application from the prior art.

The Office Action in the second full paragraph on page 4 of the Office Action reasserts that Ogle discloses how the self-polymerization of glutaraldehyde can be controlled. But the Office Action fails to explain how this control of self-polymerization as disclosed in Ogle et al., can be used in the context of the present invention to control polymerization of glutaraldehyde. All that Ogle et al. discloses is a membrane separation process for separating glutaraldehyde according to chain length.

The purpose of the separation process of Ogle et al. is to obtain "a fairly narrow distribution of oligomers sizes centered near a desired oligomer size." Column 6, lines 64-65. The membrane separation process reduces the quantity of monomers and small oligomers from entering the desired cross linking solution (the fairly narrow distribution of the oligomers sizes).

In addition, the membrane excludes undesirable large oligomers. The monomers and small oligomers are undesirable since their chain length is not sufficient for tissue fixation. The large oligomers are undesirable since they do not readily polymerize probably due to steric hindrance.

What is left is a fairly narrow distribution of a highly reactive glutaraldehyde fraction. How this fraction can be controlled for use in the present invention, or how the other excluded fractions could be controlled and used in the present invention, is not explained by the Office Action. More importantly, where is the motivation or the suggestion in Ogle et al. to use such fractions (and which specific fraction) as bridges if there is no explanation on how the reactivity of such fraction can be controlled for use in the present invention?

For glutaraldehyde, applicant's attorney has stated that it can not act as a bridge due to its reactivity with itself. This is supported by Ogle et al. being able to isolate a highly reactive fraction of glutaraldehyde and the article by John A. Kiemner (cited previously by applicant's attorney.) Therefore, the claims, as written, exclude glutaraldehyde as a bridge since glutaraldehyde reacts with glutaraldehyde.

The Office Action further states that "reacting glutaraldehyde with tissue as disclosed by Ogle et al. and then reacting with diamine as suggested by Yang et al., the diamine can be the bridge and glutaraldehyde the linker." Id at 4.

However, the Office Action does not provide any indication as to the suggestion or the motivation either in Yang et al. or Ogle et al. to combine the two to make such an invention. What is clear is that the Office Action is using applicant's claim as a guide to combine the two references. Neither the Ogle et al. or the Yang et al. patents describe linkers bonded to tissue and bridges bonded to two or more linkers wherein the linkers and the bridges are chemically

different and the functional groups of the bridges are generally non-reactive with other bridges.

As discussed previously, Ogle et al. describe a separation process for making a fairly narrow distribution of a certain chain length of glutaraldehyde for high reactivity. The Yang et al. patent describes a method of glutaraldehyde cross-linking of tissue which has been initially cross-linked with glutaraldehyde and then is subjected to a diamine, resulting in a non-carboxyl side group containing a free functional amino group for subsequent cross-linking in another rinse of glutaraldehyde. The Yang et al. reaction provides for "formation of additional glutaraldehyde cross-linkages which effect the overall cross-linked density in long-term durability of the prosthesis." Column 6, lines 35-39 of Yang et al. The whole purpose of the Yang et al. invention as illustrated in Figure 2 is to increase cross-linking density (Column 5, lines 21-26) and not to make bridges. Making bridges is antithetical to increasing cross-linking density to increase durability. Prior art references have to be looked at fairly as a whole. It is not permissible to pick and choose elements from a prior art reference to meet the claims being reviewed.

Regarding the Examiner's last comment at the top of page 5 that since "the present specification does not mention glutaraldehyde as a bridge and discloses glutaraldehyde as a linker, there is no disclosure that glutaraldehyde can not be a bridge." This comment is not understood. No disclosure is needed that glutaraldehyde cannot be a bridge since the chemistry of glutaraldehyde eliminates it as a bridge.

Regarding the Examiner's rejections under 35 U.S.C. §103, which is a repetition of the rejections in previous Office Actions, applicant once again would like to point out that Ogle et al. simply discloses a separation process in which a fairly narrow chain length range of glutaraldehyde is disclosed which

readily self polymerizes and cross links with tissue. Yang et al., as discussed above, discloses cross linking tissue with glutaraldehyde; then reacting with a diamine in such a manner that leaves a diamine with a free-functional amino group; and then subsequently cross linking further with glutaraldehyde to increase the cross linked density of the tissue. The Office Action asserts that such a reaction will leave the diamine as a linker and the glutaraldehyde being a bridge. The Examiner comments again, that "aldehyde groups of glutaraldehyde are generally non-reactive with other aldehyde groups of another glutaraldehyde under certain conditions disclosed by Ogle et al. that control self polymerizing". It is requested that these certain conditions as disclosed by Ogle et al. for control of self polymerization be identified and how they would be used in the context of the present invention be explained.

In view of the above, it is respectfully requested that the claims be reconsidered and allowed.

The Director is authorized to charge any fee deficiency required by this paper or credit any overpayment to Deposit Account No. 23-1123.

Respectfully submitted,

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